



EUROPEAN COMMISSION
JOINT RESEARCH CENTRE

Directorate F - Health, Consumers & Reference Materials (Ispra)
Health in Society

European Commission Initiative on Breast Cancer (ECIBC): European guidelines on breast cancer screening and diagnosis Evidence profile

Healthcare question	Should conventional staging exams vs. no staging exams be used for patients with clinical stage II breast cancer without symptoms suggestive of metastases?
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Abbreviations	CI: Confidence interval

Certainty assessment							Impact	Certainty	Importance
Nº of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations			
Detection rate: Combined tests (prevalence)									
6 1,2,3,4,5,6	randomised trials	serious a,b,c	not serious	serious ^d	not serious	none	Pooled detection rate: 25 per 1,000 examinations (95% CI: 13 - 41); n/N = 48/2,262	⊕⊕○○ LOW	CRITICAL
False positive: Combined tests									
3 ^{1,5,6}	randomised trials	serious a,b,c	not serious	serious ^d	not serious	none	Pooled false positive: 53 per 1,000 examinations (95% CI: 16 - 109); n/N = 72/1,600	⊕⊕○○ LOW	CRITICAL

Certainty assessment							Impact	Certainty	Importance
Nº of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations			
Detection rate: Bone Scan									
5 ^{2,3,5,7,8}	randomised trials	serious _{a,b,e}	not serious	serious ^d	not serious	none	Pooled detection rate: 21 per 1,000 examinations (95% CI: 9 - 38); n/N = 61/4,597	⊕⊕○○ LOW	CRITICAL
False positive: Bone Scan									
1 ⁵	randomised trials	serious _{a,b,e}	not serious	not serious	not serious	none	False positive: 101 per 1,000 examinations (95% CI: 62 - 160); n/N = 15/148	⊕⊕⊕○ MODERATE	CRITICAL
Detection rate: CT Chest									
2 ^{3,9}	randomised trials	serious _{a,b,e}	not serious	serious ^d	not serious	none	Pooled detection rate: 0 per 1,000 examinations (95% CI: 0 - 0); n/N = 4/871	⊕⊕○○ LOW	CRITICAL
False positive: CT Chest									
1 ⁹	randomised trials	serious _{a,e}	not serious	not serious	not serious	none	False positive: 144 per 1,000 examinations (95% CI: 122 - 170); n/N = 121/838	⊕⊕⊕○ MODERATE	CRITICAL
Detection rate: CT pelvic									
1 ³	randomised trials	serious _{a,b,e}	not serious	serious ^d	serious ^f	none	Detection rate: 53 per 1,000 examinations (95% CI: 6 - 177); n/N = 2/38	⊕○○○ VERY LOW	
False positive: CT Pelvic - not reported									
-	-	-	-	-	-	-		-	CRITICAL
Detection rate: CT abdominal									
1 ³	randomised trials	serious _{a,b,e}	not serious	serious ^d	serious ^f	none	Detection rate: 86 per 1,000 examinations (95% CI: 29 - 190); n/N = 5/58	⊕○○○ VERY LOW	CRITICAL
False positive: CT abdominal - not reported									
-	-	-	-	-	-	-		-	CRITICAL
Detection rate. RX Chest									
2 ^{2,3}	randomised trials	serious ^a	not serious	serious ^d	serious ^f	none	Pooled detection rate: 12 per 1,000 examinations (95% CI: 2 - 28); n/N = 6/345	⊕○○○ VERY LOW	CRITICAL
False Positive: RX Chest - not reported									
-	-	-	-	-	-	-		-	CRITICAL
Detection rate: US									
3 ^{2,3,5}	randomised trials	serious _{a,b,e}	not serious	not serious	not serious	none	Pooled detection rate: 3 per 1,000 examinations (95% CI: 0 - 14); n/N = 2/372	⊕⊕⊕○ MODERATE	CRITICAL
False positive: US									
1 ⁵	randomised trials	serious _{a,b,e}	not serious	not serious	not serious	none	False positive: 34 per 1,000 examinations (95% CI: 14 - 77); n/N = 5/148	⊕⊕⊕○ MODERATE	CRITICAL

Explanations

- a. Different reference standards were used, some included another imaging test without histological confirmation which is likely to incorrectly classify the condition.
- b. Some studies included retrospective case records where inclusion criteria cannot be properly assessed, in some cases the distribution of stages at diagnosis is not that expected in the population, in particular stage I and stage II are under-represented; this suggest that only a subpopulation of these cases entered in the study and that they could be those with higher suspicious of having distal metastases.
- c. The proportion of patients actually staging investigated with more than one imaging tests was variable which could underestimated the exams ' performance. All studies reported to include follow-up of patients although with different time frame.
- d. Some or most of the studies recruited consecutive patients from medical records (or prospectively) who could or could not have symptoms suggestive of metastases.
- e. The assessment of each individual tests is based in the number of patients that were examined who are a subpopulation of all those subject at this stage which could overestimate its performance measurements.
- f. Judgement of imprecision was considered serious as one or both of the confidence interval limits reached detection rates threshold which could potentially change the decision about requesting staging tests.

References

1. Bychkovsky BL, Guo H,Sutton J, Spring L,Faig J,Dagogo-Jack I,Battelli C,Houlihan MJ,Yeh TC,Come SE,Lin NU.. Use and Yield of Baseline Imaging and Laboratory Testing in Stage II Breast Cancer. *Oncologist*.; 2006.
2. Puglisi F, Follador A,Minisini AM,Cardellino GG,Russo S,Andreetta C,Di Terlizzi S,Piga A.. Baseline staging tests after a new diagnosis of breast cancer: further evidence of their limited indications. *Ann Oncol*.; 2005.
3. Dillman RO, Chico S. Radiologic tests after a new diagnosis of breast cancer.. *Eff Clin Pract*.; 2000.
4. Ravaioli A, Tassinari D,Pasini G,Polselli A,Papi M,Fattori PP,Pasquini E,Masi A,Alessandrini F,Canuti D,Panzini I,Drudi G.. Staging of breast cancer: what standards should be used in research and clinical practice? *Ann Oncol*. ; 1998.
5. Kasem AR, Desai A,Daniell S,Sinha P.. Bone scan and liver ultrasound scan in the preoperative staging for primary breast cancer. *Breast J*; 2006.
6. Barret T, Bowden DJ,Greenberg DC,Brown CH,Wishart PD. Radiological staging in breast cancer: which asymptomatic patients to image and how. *Br J Cancer*; 2009.
7. Koizumi M, Yoshimoto M,Kasumi F,Ogata E.. What do breast cancer patients benefit from staging bone scintigraphy? *Jpn J Clin Oncol*.; 2001.
8. Lee JE, Park SS,Han W,Kim SW,Shin HJ,Choe KJ,Oh SK,Youn YK,Noh DY,Kim SW.. The clinical use of staging bone scan in patients with breast carcinoma: reevaluation by the 2003 American Joint Committee on Cancer staging system. *Cancer*. ; 2005.
9. Kim H, Han W,Moon HG,Min J,Ahn SK,Kim TY,Im SA,Oh DY,Han SW,Chie EK,Ha SW,Noh DY.. The value of preoperative staging chest computed tomography to detect asymptomatic lung and liver metastasis in patients with primary breast carcinoma. *Breast Cancer Res Treat*.; 2011.